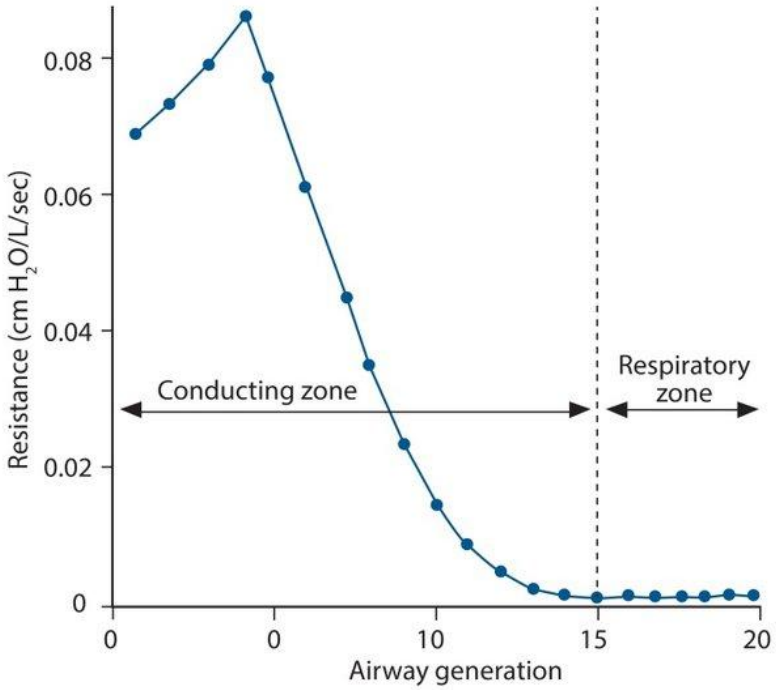
Respiratory System Physiology

Comprehensive File 3 – V1

Dr. Yanal Shafagoj



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As introduced in lecture 1, lung diseases are divided into 3 parts:

- 70% are of obstructive pattern – COPD: chronic bronchitis, emphysema, with or without asthma.
- 20% are of restrictive pattern – problems in the expansion of alveoli seen in pulmonary fibrosis, pulmonary edema, infant respiratory distress syndrome (IRDS), and acute respiratory distress syndrome (ARDS); the last two show a huge tendency for the alveoli to collapse.
- 10% are of vascular causes.

Other non-lung related causes of hypoxia include the following:

- Anemia and hemoglobinopathies.
- Heart failure.
- Paralysis of the respiratory muscles, as in poliomyelitis affecting the phrenic nerves. Drug overdoses can depress the respiratory center in medulla oblongata.

Airways Resistance

As discussed previously, a driving force of +1 mmHg is enough for respiration to happen; remember that $\boldsymbol{Flow} = \frac{\boldsymbol{P_{atm} - P_{alveolar}}}{\boldsymbol{R_{airways}}}$. [DF = $P_{alveolar} - P_{atm}$ for expiration.]

This flow (RMV) can also be calculated using the following equation:

$$\boldsymbol{Respiratory\ minute\ ventilation\ (RMV) = Tidal\ volume\ (V_T) \times Respiration\ Rate\ (RR)}$$

$$\boldsymbol{Respiratory\ minute\ ventilation\ (RMV) = 0.5\ L \times 12\ \frac{breathes}{min} = 6\ \frac{L}{min}}$$

Remember that $\boldsymbol{Cardiac\ output\ (Q) = Stroke\ volume * Heart\ rate \approx 5\ \frac{L}{min}}$.

Notice how the two flow values are close; to achieve a flow (Q) of 5 L/min, the heart provides a driving force of 100 mmHg mean arterial pressure against the total peripheral vascular resistance. Recall that the arterioles contribute the most for the resistance, and this is evident since they require the largest pressure gradient to maintain the flow.

Back to the lungs, beware that $R \propto \frac{1}{A^2}$ [Recall that $R \propto \frac{1}{r^4}$ and that $A \propto r^2$].

The air flow required only +1 mmHg of driving force to achieve a normal RMV; this means that airway resistance is equal to 1% of the total peripheral vascular resistance, given that both flows are close enough (5 ≈ 6).

How is the Resistance Measured?

Resistance can be directly measured with the following equation: $\boldsymbol{R = \frac{8\eta l}{\pi r^4}}$.

However, for this equation to be used, three conditions must be met.

- The fluid must be homogenous, while blood contains different components.
- The flow must be steady, not pulsatile.
- The flow must be laminar, not turbulent.

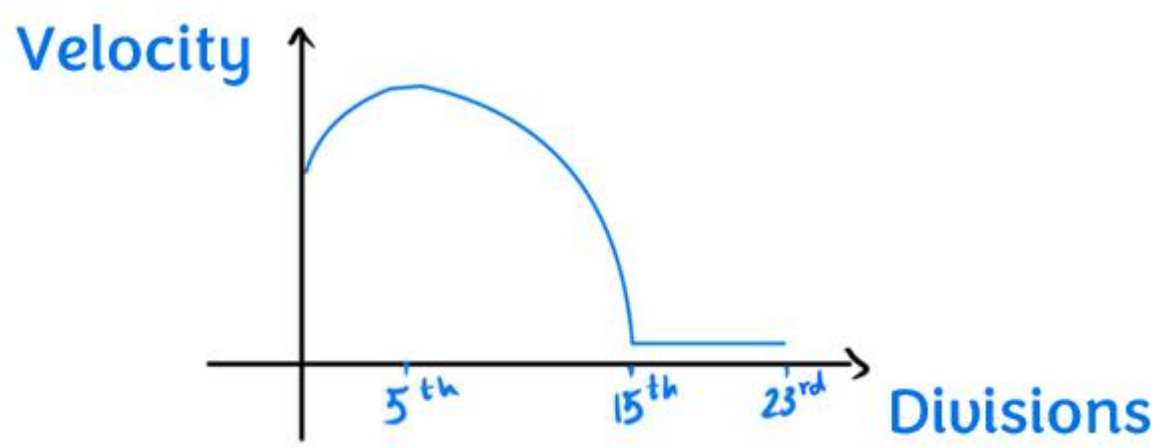
These conditions cannot be met in physiological hemo/aerodynamics.
It is also difficult for 'l' and 'r' to be measured, as we have 23 divisions through the lung.

The resistance can be **indirectly** measured by this equation:

$$\boldsymbol{R = \frac{DF}{Flow} = \frac{1\ mmHg}{6\ \frac{L}{min}} \rightarrow too\ small}$$

The airway resistance is physiologically small, yet it is important to know where exactly in the respiratory tract it resides. Remember that $\boldsymbol{Velocity\left(\frac{d}{t}\right) = \frac{Flow\left(\frac{d^3}{t}\right)}{Area\ (d^2)}}$.

Plotting the velocity of air against lung divisions gives us the following figure:



When the velocity of air is high, the (total division-specific) cross-sectional area is small, and thus the resistance in high. This means that nearly 40% of the airway resistance contribution is from airways above the larynx, another 40% of resistance is present in the first 4 divisions, and the last 20% of resistance is present in the rest of divisions where the velocity becomes very low and almost reaches zero.

So, most of the airway resistance normally resides in the larger divisions.

Pathological Airway Resistance

In pathological conditions that show increased airway resistance, which parts of the airways contribute most to this increased resistance?

The large airways are surrounded by cartilage that prevents them from collapsing, and they are, by definition, larger, so accumulation of mucus, for example, will not significantly narrow them. On the other hand, smaller divisions lack supporting cartilage and have narrower diameters, making them vulnerable to significant obstruction by mucus.

Clinically, mucolytic drugs are given to dissolve the mucus and aid in its removal, and this maintains smaller divisions patent. Remember that mucus is composed of organic compounds (primarily glycoproteins) and water. When water is reabsorbed from the accumulated mucus, only the hard part stays, which is why drugs are needed.

Coughing reflexes are of great importance here, and this is why drugs that stop coughing are contraindicated in patients with productive cough. They are also contraindicated in children as children usually cannot express their exact symptoms.

Smoking worsens this case by many ways, including increasing mucus secretion by goblet cells, and paralyzing the cilia, which normally remove mucus outside the respiratory tract.

In addition to the absence of cartilage and the narrow diameter, smaller air ways have more smooth muscle content, which makes them more vulnerable to severe bronchoconstriction, which is induced by several inflammatory mediators such as leukotrienes, prostaglandins, and histamine. This is primarily what happens in asthma.

All these facts explain why smaller airways, not larger ones, are responsible for increased airway resistance in pulmonary diseases.

During what phase does high airway resistance show up more?

As mentioned before, obstructive pulmonary diseases mainly show difficulty in exhaling, not inhaling. This is mainly because of intrapleural pressure changes. Higher intrapleural pressure, which is the case during exhalation, causes the collapse of the airways, further exacerbating the obstruction in addition to the aforementioned causes.

Because the resistance increases the required driving force to maintain normal flow, additional work must be done to increase intrapleural pressure during exhalation. This fact makes exhalation a “paid” process, increasing energy expenditure significantly above the normal 2%. Note that $\boldsymbol{Work} = \Delta \boldsymbol{P} * \Delta \boldsymbol{V};\ \Delta P = DF;\ \Delta V = Tidal\ Volume.$

This difficulty in exhalation shows as a wheezing sound, which varies with severity.

To quantify things, imagine that the lungs need an intra-alveolar pressure of +10 mmHg instead of the normal +1 mmHg for expiration. This means that the ΔP has increased 10 times, which will in turn increase the work done 10 times, and this will raise the energy expenditure from 2% to 20% of the total ATP. In such cases, the lungs are no more an efficient machine, and the patient will suffer of fatigue proportional to the degree of obstruction; more obstruction → more R → increased required ΔP → more work done.

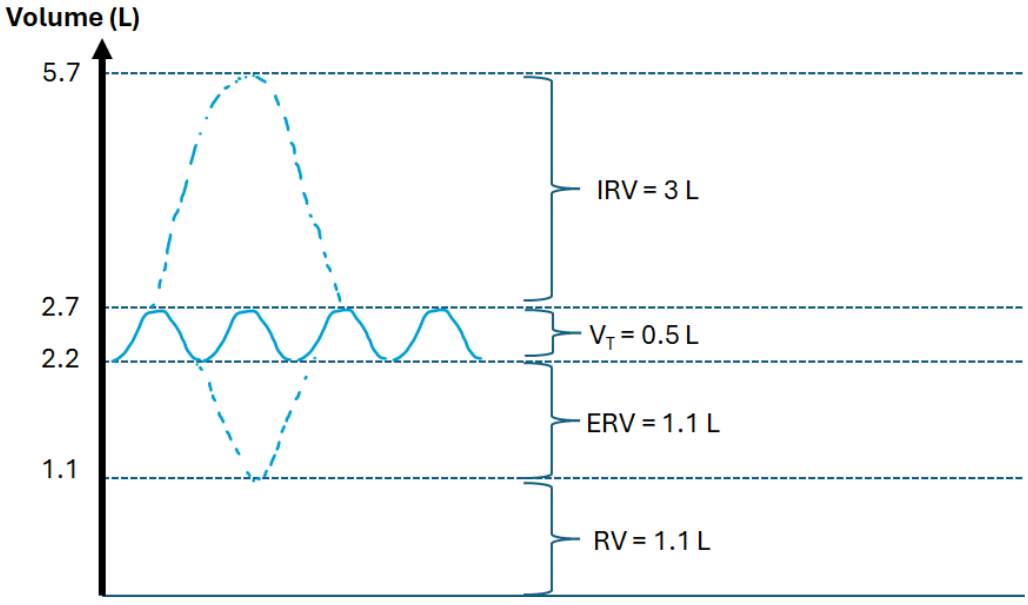
Inhalation, on the other hand, decreases intrapleural pressure and causes the opening of the airways. This is why inhalation is easier than exhalation in obstructive diseases.

Restrictive lung disease, as discussed before, shows difficulty in inhalation due to increased collapsing forces or decreased compliance of the alveoli to fill in air.

The resting volume of the lungs, at which the lungs (excluding the airways) no longer tend to collapse, is approximately 150 ml. This is analogous to a rubber band returning to its resting length once all external forces are removed.

Volumes and Capacities of the Lungs

The figure below shows the 4 important lung volumes and their definitions.



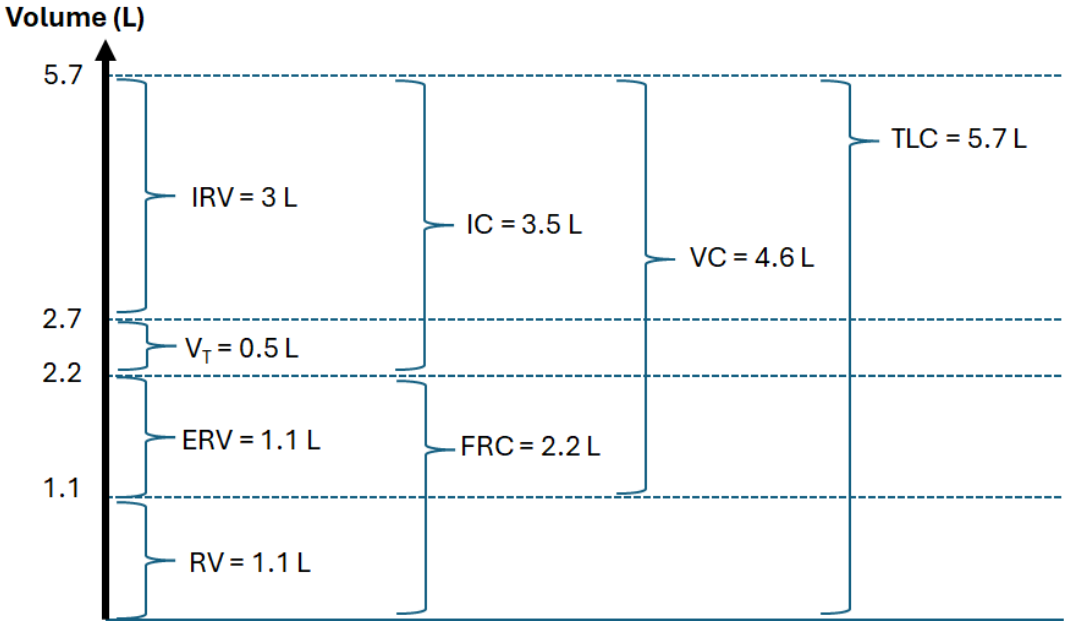
Tidal Volume (V_T): volume of air inspired or expired during a normal breath.

Inspiratory Reserve Volume (IRV): maximum volume of air that can be inspired after a normal inspiration; reflects inspiratory muscle strength and lung compliance.

Expiratory Reserve Volume (ERV): maximum additional volume of air that can be expired after a normal tidal expiration; depends on expiratory muscle effort.

Residual Volume (RV): air remaining in the lungs after a maximal forced expiration.

The following figure shows all 4 volumes and 4 capacities (sum of volumes) of the lungs and their approximate physiological values.



Inspiratory Capacity (IC): the maximum volume of air that can be inspired starting from the end of a normal expiration; it equals **V_T + IRV**.

Functional Residual Capacity (FRC): the volume of air remaining in the lungs at the end of a normal, passive expiration; it equals **ERV + RV**.

Vital Capacity (VC): the maximum volume of air that can be expelled forcefully following a maximal inspiration; it equals **IRV + V_T + ERV (all volumes except RV).**

Total Lung Capacity (TLC): the total volume of air in the lungs after a maximal inspiration; it equals **VC + RV (all 4 volumes)**.

Residual volume (RV) is not the same as the resting lung volume (150 mL). RV is the volume of air remaining in the lungs after maximal forced expiration (1100 mL), mainly due to airway closure and gas trapping. In contrast, the resting lung volume is a theoretical volume reflecting the lung's intrinsic elastic equilibrium if all distending forces were removed, which does not happen in physiological conditions. The resting lung volume is about 150 ml (not zero because of air trapping). Thus, RV is a measured physiological volume, whereas the resting lung volume is a property of lung elasticity, and they are fundamentally different.

All volumes and capacities, except those depending on RV, can be calculated using a spirometer. RV, TLC, and FRC need other methods. FRC calculation is shown next.

Measurement of Functional Residual Capacity (FRC)

Helium Dilution Method

The helium dilution method is based on the principle of conservation of mass.
Helium (He) is an inert, insoluble gas that:

- Does **not** diffuse across the alveolar–capillary membrane
- Is **not** absorbed into blood

Therefore, when a known amount of helium is allowed to mix with the gas in the lungs, the **degree of helium dilution** can be used to calculate the unknown lung volume, which is the functional residual capacity (FRC).

1. A system (analogous to a breathing bag) is filled with a known gas volume ($\mathbf{V_1}$) containing helium at a known concentration ($\mathbf{C_1}$).
2. The patient is connected to the system **at the end of a normal expiration**, when lung volume equals **FRC**.
3. The subject breathes normally from the closed system.
4. Helium gradually mixes between the spirometer gas and the lung gas.
5. After equilibration, the helium concentration becomes uniform and is measured as the **final concentration ($\mathbf{C_2}$)**.

Conservation of helium:

$$\text{Initial amount of He} = \text{Final amount of He}$$

$$\boldsymbol{C_1 \times V_1 = C_2 \times (V_1 + FRC)}$$

Final Equation:

$$\boldsymbol{FRC = V_1 \left(\frac{C_1}{C_2} - 1\right)}$$

A **greater drop** in helium concentration (C_2 much less than C_1) indicates a **larger FRC**.

A **small change** in helium concentration indicates a **smaller FRC**.

Changes from VERSION 0 to VERSION 1:

- Added page **7** (FRC calculations)
- Clarified more about the resting lung volume and differentiating it from residual volume (in page **6**)